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REMARKS

In response to the final office action dated August 19, 2005, Applicants respectfully request reconsideration based on the above claim amendment and the following remarks. Applicants respectfully submit that the claims as presented are in condition for allowance.

Claims 1-13 are present for consideration.

As explained below, Applicants believe they have placed the claims in condition for allowance according to 37 C.F.R. 1.116, and respectfully request reconsideration and allowance of the claims in view of the above amendments and the following remarks.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 3 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office Action states that it is unclear what is meant by the phrase "a terminal of nucleic acids". Claim 3 is amended to read "a terminal of a nucleic acid".

In view of this clarifying amendment, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 3 under 35 U.S.C. § 112, second paragraph.

Claim Rejections Under 35 U.S.C. § 102(b)

Claims 1-2, 5-8 and 11-12 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Cantor et al (US Patent No. 5,795,714). Applicants respectfully traverse this rejection.

To anticipate a claim, a reference must disclose each and every element of the claim. *Lewmar Marine v. Varient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987).

The manufacturing a template nucleic acid array step in Applicants pending claim 1 is as follows:

> "(a) manufacturing a template nucleic acid array by immobilizing on a surface of a first substrate first nucleic acid probes, each of which includes a first polynucleotide that has a sequence complementary to a second polynucleotide to be synthesized and a primer binding site;

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wherein immobilizing one of the first nucleic acid probes comprises bringing a protruding portion of the first substrate into contact with a solution of the first nucleic acid probe filling a recessed portion of another uneven substrate such that the first nucleic acid probe is immobilized on the surface of the protruding portion of the first substrate".

In this step, the *template* nucleic acid array is manufactured. In manufacturing the template array, a first nucleic acid probe is immobilized on a surface of a first substrate by bringing a protruding portion of the first substrate into contact with the first nucleic acid probe which is in a solution in a recessed portion of another uneven substrate. The contact between the protruding portion and the first nucleic acid probe in solution is such that the first nucleic acid probe is immobilized on the surface of the protruding portion.

The Office Action, on p.5, states that Cantor et al. anticipate the method of claim 1 because "Cantor et al. teach a master array of beads able to be manipulated in microtiter plates (i.e. recessed portion of another uneven substrate)" (col. 21, lines 29-30) and also teach "a master array consisting of a set of streptavidin bead-impregnated plastic coated metal pins (i.e., protruding portion), each of which, at its tip, contains immobilized biotinylated DNA strands (Column 21, lines 59-63)". The Office Action further states that Cantor et al. teach transfer of the newly synthesized 5'-biotinylated from the master array to the streptavidin-coated replica surface at col. 22, lines 1-3).

Applicants disagree with this anticipation rejection. Cantor et al. teach an array of magnetic microbeads with *attached* oligonucleotides that can be manipulated in microtiter plates (col 21, lines 29-30), however the oligonucleotides present in the recessed portions of the microtiter plate are not free in solution but are instead *immobilized* on the magnetic microbeads. Cantor et al. teach creating a master array, i.e., a template array, of oligonucleotides by printing it with multiple headed pipettes (col 21, lines 51-52), but Cantor et al. do not teach immobilizing nucleic acids on a substrate surface in manufacturing a master array on a substrate by bringing a protruding portion of the substrate into contact with an oligonculeotide solution in a recessed portion of another substrate. Cantor et al. teach creating *replica* arrays by incubating the *master* array, with a set of streptavidin bead-impregnated plastic coated metal pins, with complementary 5'-biotinylated sequences to permit subsequent DNA synthesis (Col. 21, line 59 to col. 22, line 1),

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but Applicants can find no teaching in Cantor et al. corresponding to manufacturing a *template* array by immobilizing nucleic acid probes on a first substrate surface wherein "immobilizing one of the first nucleic acid probes comprises bringing a protruding portion of the first substrate into contact with a solution of the first nucleic acid probe filling a recessed portion of another uneven substrate such that the first nucleic acid probe is immobilized on the surface of the protruding portion of the first substrate".

Consequently, Cantor et al. do not anticipate Applicants' amended claim 1 because Cantor et al. do not teach all the elements of Applicants' claim 1. Given that claims 2, 5-8 and 11-12 each include or further limit all of the elements of claim 1, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-2, 5-8 and 11-12 under 35 U.S.C. § 102(b) over Cantor et al.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 3-4, 9-10, and 13 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Cantor et al (U.S. Patent No. 5,795,714) in view of Dickinson et al (U.S. Patent No. 6,770,441). Applicants respectfully traverse this rejection.

For an obviousness rejection to be proper, the Examiner must meet the burden of establishing a *prima facie* case of obviousness, i.e., that all elements of the invention are disclosed in the prior art; that the prior art relied upon, coupled with knowledge generally available in the art at the time of the invention, contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or combined references; and that the proposed modification of the prior art had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was make. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In Re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970); *Amgen v. Chugai Pharmaceuticals Co.*, 927 U.S.P.Q.2d, 1016, 1023 (Fed. Cir. 1996).

Applicants argue that the Examiner has failed to establish a *prima facie* case of obviousness of claims 3-4, 9-10, and 13, and therefore, the obviousness rejection under 35 U.S.C. §103(a) is improper because all elements of the invention are not disclosed in the cited references.

Claims 3-4 and 9-10 each include or further limit all of the elements of claim 1. Therefore for an obviousness rejection of claims 3-4 and 9-10 over Cantor et al. in view of Dickenson et al.,

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Cantor et al. and Dickinson et al. must disclose all the elements of amended claim 1 and also those of claims 3-4 and 9-10

As discussed above in the traversal of the §102(b) rejection of claim 1 over Cantor et al., Cantor et al. fail to teach at least the following element of claim 1:

> "(a) manufacturing a template nucleic acid array by immobilizing on a surface of a first substrate first nucleic acid probes, each of which includes a first polynucleotide that has a sequence complementary to a second polynucleotide to be synthesized and a primer binding site;
>
> wherein immobilizing one of the first nucleic acid probes comprises bringing a protruding portion of the first substrate into contact with a solution of the first nucleic acid probe filling a recessed portion of another uneven substrate such that the first nucleic acid probe is immobilized on the surface of the protruding portion of the first substrate".

Since Cantor et al. neither teach nor suggest this element of claim 1, Dickinson et al. must teach or suggest this element for the obviousness rejection to be proper. As noted in the response filed July 29, 2005, Dickinson et al. teach a submaster structure with protruding portions that is used to form a molded layer (Fig 14A, part 310; col. 4, lines 1-10), however Applicants cannot find any statement in Dickinson et al. that teaches or suggests bringing a protruding portion of this submaster structure into contact with a nucleic acid probe solution such that the nucleic acid probe is immobilized on the surface of the protruding portion of the submaster structure. Consequently, as the combination of Cantor et al. and Dickinson et al. fail to teach or suggest each element of independent claim 1, from which claims 3-4 and 9-10 depend, Applicants assert that a *prima facie* case of obviousness has not been established for claims 3-4 and 9-10 over Cantor et al. in view of Dickinson et al.

Applicants' independent claim 13 reads as follows (emphasis added):

13. (Previously presented) A method of replicating a nucleic acid array, the method comprising:

(a) immobilizing first nucleic acid probes on a surface of a previously patterned first substrate to manufacture a template nucleic acid array,

wherein each of the first nucleic acid probes includes a first polynucleotide that has a

sequence complementary to a second polynucleotide to be synthesized and a primer binding site;

wherein immobilizing one of the first nucleic acid probes comprises

filling a recessed portion of another uneven substrate with a solution of a first nucleic acid probe, and

bringing a protruding portion of the first substrate into contact with the solution such that the first nucleic acid probe is immobilized on the surface of the protruding portion of the first substrate;

(b) binding a plurality of primers to the primer binding sites of the immobilized first nucleic acid probes;

(c) in-situ synthesizing the second polynucleotide, initiating from at least one of the primers using the first polynucleotide as a template; and

(d) transferring second nucleic acid probes, each of which includes the second polynucleotide and the primer, to a second substrate from the first substrate.

As discussed previously regarding claim 1, although Cantor et al. do teach *magnetic microbeads with attached oligonucleotides* that can be manipulated in microtiter plates (col 21, lines 29-30), the oligonucleotides present in the recessed portions of the microtiter plate are not free in solution but are immobilized on the microbeads. Applicants can find no teaching in Cantor et al. corresponding to immobilizing first nucleic acid probes on a surface of a previously patterned first substrate *to manufacture a template nucleic acid array, "wherein immobilizing one of the first nucleic acid probes comprises*

filling a recessed portion of another uneven substrate with a solution of a first nucleic acid probe, and

bringing a protruding portion of the first substrate into contact with the solution such that the first nucleic acid probe is immobilized on the surface of the protruding portion of the first substrate".

Since Cantor et al. neither teach nor suggest these elements of claim 13, Dickinson et al. must teach or suggest these elements for the obviousness rejection to be proper. As noted above, Dickinson et al. teach a submaster structure with protruding portions that is used to form a molded layer (Fig 14A, part 310; col. 4, lines 1-10), however Applicants cannot find any statement in Dickinson et al. that teaches or suggests bringing a protruding portion of this submaster structure

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into contact with a nucleic acid probe solution such that the nucleic acid probe is immobilized on the surface of the protruding portion of the submaster structure. Consequently, as the combination of Cantor et al. and Dickinson et al. fail to teach or suggest each element of claim 13, Applicants assert that a *prima facie* case of obviousness over Cantor et al. in view of Dickinson et al. has not been established for claim 13.

Further, even assuming that all elements of an invention are disclosed in the prior art, an Examiner cannot establish obviousness by locating references that describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would have impelled one skilled in the art to do what the patent applicant has done. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. Int. 1993).

The Office Action has failed to make any statement regarding the motivation to combine Cantor et al. with Dickinson et al. Absent motivation to change Cantor et al. with elements provided by Dickinson et al., no *prima facie* case of obviousness has been established for claims 3-4, 9-10, and 13.

In view of the above arguments, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 3-4, 9-10, and 13.

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It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance is requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130 maintained by Applicants' attorneys.

Respectfully submitted,

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